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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,292	07/05/2005	Susumu Muto	P26318	5595

7055 7590 05/14/2009

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EXAMINER
RAE, CHARLESWORTH E

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
05/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/516,292	MUTO ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,29 and 34-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 29, 34-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/06/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 01/06/09, have been fully considered but they are not deemed to be persuasive.

Status of the Claims

Claims 1 and 29, 34-41 are currently pending in this application

Claims 1, 29, and 34-41 are currently under examination.

Foreign Priority

It is noted that an English translation of the priority document has not been filed (see Office action, mailed 01/08/08, page 2). Hence, for examination purposes, the effective filing date for the instant application for art rejection purposes is the filing date of the application under 371, which is 06/05/03.

Miscellaneous

In response to applicant's request for clarification of the status of the application, it is noted that the status of the application as it appears in PAIR is correct. It is noted that the status of the application was inadvertently stated as "Final" on Form 326, mailed 10/06/08. Form 326, mailed 10/06/08, is hereby amended to correct the inadvertent error.

The examiner wishes to thank applicant for pointing out the error and apologize for any inconvenience that the error might have caused.

Response to applicant's arguments

Scope of enablement rejection under 112, 1st paragraph

This rejection is withdrawn in view of the claim amendment and applicant's persuasive arguments (see applicant's Response, pages 26-27.

Lack of written description rejection under 112, 1st paragraph

This rejection is withdrawn in view of the claim amendment.

REJECTIONS

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

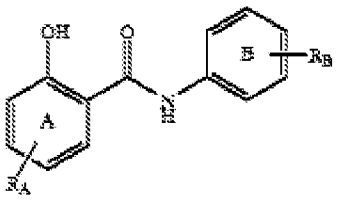
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 29, and 34-40 are rejected under 103(a) as being unpatentable over Callahan et al. (US Patent 6,492,425), in view of Sasaki et al. (Sasaki et al. The anthelmintic Drug mebendazole induces mitotic arrest and apoptosis by depolymerizing tubulion in non-small cell lung cancer cells. Molecular Cancer Therapeutics. November, 2002: 1201-1209), and further in view of Franz et al. (US Patent 3,906,034).

Callahan et al. (6,492,425) teach of methods of treating cancer comprising compounds wherein a major portion of said compounds is identical to the instant claimed compounds. Callahan et al. teach the below inhibitory compounds of transcription factor NF-κB and methods of treatment of a variety of diseases associated with NF-κB activation in a patient in need of treating, including cancer (e.g. Hodgkin's disease) and restenosis, wherein the patient includes human (see abstract, and col. 3, line 17 to col. 4, line 54; see especially reference claim 1):

I



wherein:

R_A substitutes ring A 0–3 times and is independently selected from the group consisting of: NO_2, halogen, C_{1-6}alkyl, trifluoromethyl, O—C_{1-6}alkyl and S—C_{1-6}alkyl; and

R_B substitutes ring B 0–3 times and is independently selected from the group consisting of: halogen,C(O)

C_{1-6}alkyl, C_{1-6}alkyl, O—C_{1-6}alkyl, S—C_{1-6}alkyl, CH_2-aryl, and aryl;

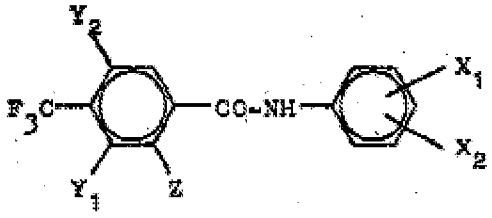
The compounds of Callahan et al. overlaps with the instant claims when Ra (of the A ring, equivalent to the instant claimed Z ring) is halogen.

However, Callahan et al. do not teach applicant's elected compound having two CF3 substituents, or the specific instantly claimed cancers.

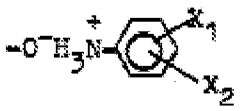
Sasaki et al. report that mebendazole induced depolymerization of tubulin and inhibited normal spindle formation in non-small cell lung cancer (NSCLC) cells, resulting in mitotic arrest and cell death (page 1206, col. 2, first full para.). Sasaki et al. state that mebendazole also induced apoptosis in NSCLC cells after mitotic arrest (page 1206, 3rd para.). However, Sasaki et al. teach that mebendazole has less an effect on mitotic spindle formation and in the depolymerization of tubulin in tumors cells as compared with the well known spindle inhibitor, nocodazole (page 1208, last para.). Sasaki et al. state that studies of schedule administration and side effects of mebendazole in the treatment of cancer or investigations of the use of mebendazole in combination with

other chemotherapeutic agents will further elucidate the potential usefulness of mebendazole as an anticancer drug (page 1208, last para.).

Franz et al. (US Patent 3,906,034) teach compounds having the below general structure and methods comprising administering said compounds either orally or subcutaneously for treating warm blooded animals suffering from helminthiasis (abstract; col. 3, line 24 to col. 4, line 26:



in which X_1 and X_2 each represent hydrogen, chlorine, methyl or trifluoromethyl, Y_1 and Y_2 each represent hydrogen, chlorine or the nitrogroup, at least one of the substituents Y_1 and Y_2 not being hydrogen, and Z stands for —OH, —O—CO—alkyl or



The above structure taught by Franz et al. overlaps with the compounds of Callahan et al. when each X1 and X 2 as taught by Franz et al. are CF3, Y1 is hydrogen and the Y2 is chlorine, and Z is OH.

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references by manipulating the

substituents of the core structure of the compounds of Callahan et al., including arriving at the instant claimed compounds, in order to improve the anti-cancer effects of benzimidazole carbamate compounds. One would have been motivated to do so because Sasaki et al. suggest that more effective benzimidazole carbamate compounds are needed for use in the treatment of cancer as evidenced by the teaching that more studies are needed in order to use mebendazole as an anticancer drug (page 1208, last para.) and Callahan et al., and Franz et al. are directed to benzimidazole compound

It would have been obvious to a person skill in the art at the time the invention was made to combine the teachings of Callahan et al. and Sasaki et al. in order to treat a human patient with cancer (e.g. NSCLC). One would have been motivated to do so because Sasaki et al. suggest that antihelmintic benzimidazole compounds (e.g. mebendazole) induce apoptosis in cancer cells after mitotic arrest (page 1208, last para.) and the compounds taught by Callahan et al. share a common core structure to the antihelmintic compounds taught by Franz et al. and Sasaki et al. such that one would reasonably expect that compounds that share similar structures would also have similar therapeutic properties (e.g. treating cancer)..

Further, it would have been obvious to a person of skill in the art at the time the invention was made to manipulate the substituents of the core structure of the compounds of Callahan et al. in view of the teaching of Franz et al. to optimize the therapeutic profile of said compounds. One would have been motivated to do so because Franz et al. teach compounds that share a common core structure as the compounds of Callahan et al. and suggest that X1 and X2 can both be CF3, and

applicant's claimed compound also have two CF3 substituents on the phenyl ring equivalent to the phenyl ring bearing X1 and X2, and Callahan et al. teach compounds wherein the phenyl ring equivalent to the instant claimed E moiety (= phenyl ring of Franz with X1 and X2) may be substituted with 0-3 substituents such that one would reasonably expect to attempt to add the two CF3 substituents to the phenyl ring of Callahan et al. since Franz et al. suggest that X1 and X2 can be both CF3. Further, since both Franz et al. and Callahan et al. teach compounds that have similar structures that appear to retain their therapeutic properties following manipulation of the phenyl substituents, one would reasonably expect that modification of the substituents of the phenyl rings of the core structure to arrive at applicant's elected compound species would not significantly affect their therapeutic properties. Besides, Callahan et al. teach compounds that are useful for treating a variety of disorders (e.g. cancer) and Franz et al. teach compounds that are antihelminthics and benzimidazole cabarmates antihelmintics are also known to exhibit anti-tumor activity as evidenced by the teaching of Sasaki et al. that benzimidazole carbamates have been reported to inhibit the polymerization of tubulins and to disrupt the function of microtubules in parasite cells (page 1201, col. 2, second para.).

Regarding claim 1, it is noted that Sasaki et al. teach NSCLC, which overlaps with the instant claimed cancer population.

With respect to the term “administering to a mammal a therapeutically effective amount of a compound represented by ... formula I," Callahan et al. teach a method of administering a benzimidazole carbamate compound to a patient in need of NF-kB

inhibition an amount effective for inhibition of NF-kB such that one would reasonably expect that said dose would be an amount that is therapeutically effective amount.

With respect to the preamble, Sasaki et al. teach a method of treating mice with lung cancer (page 1205, last para. to page 1206, col. 1).

Regarding claim 29, one would reasonably envisage that administering of the prior art compounds to a patient in need-thereof of said treatment as taught by Callahan et al. would be a human (abstract).

Regarding claim 34, the above discussion of claim 1 is incorporated by reference. Since the prior encompass applicant's elected compound species, one would reasonably expect that the compounds encompassed by the prior art would have similar effects as claimed, including inhibiting proliferation of tumor cell or cancer cell.

Regarding claims 35-41, it is noted that the compounds encompass by the prior art overlaps with the instant claimed compounds as discussed above.

Thus, a person of skill in the art at the time the invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Response to applicant's argument

Applicant's arguments with respect to the rejection under 103(a) have been considered but are moot in view of the new ground(s) of rejection. The merits of Franz and Callahan et al. are maintained.

In response to applicant's arguments that Franz et al. is directed solely to compounds having anthelimintic action, which is completely unrelated to the teachings

of Callahan et al, is not found to be persuasive because benzimidazole carbamate antihelmintics (e.g. mebendazole) as taught by Sasaki is known to posses anti-cancer activity (page 1206, col. 2, first full para.).and the compounds of Franz et al. and Callahan et al. as discussed above are benzimidazole carbamates such that one would reasonably expect that the compounds of Franz et al. and Callahan et al. to exhibit similar utilities absent objective evidence to the contrary.

In response to applicant's argument that Callahan et al. do not teach that the compounds may be substituted with three or more halogens despite the fact that CF3 and similar substituents were known in the medicinal chemistry art, it is noted that the compounds of Franz et al. and Callahan et al. .share a common core structure and therefore modification of the substituents is obvious since both prior art references teach the same core (MPEP 2144.08-2144.09). Besides, Franz et Al. do suggest compounds having two CF3 substituents (= applicant's elected compound) and Callahan et al. teach compounds wherein Ra can be chlorine (reference claim) such that one would reasonably expect to modify the compound of Callahan et al to arrive at applicant's elected compound absent objective evidence to the contrary.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

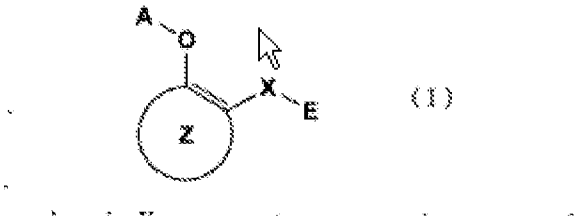
and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17, 21, 24-33 of copending U.S. Patent Application No. 10/564, 407 (appl. ‘407).

In particular, claim 1 of copending appl. '407 is directed towards a medicament for preventive and/or therapeutic treatment of dermal pigmentation and/or development of skin cancer, which comprises as an active ingredient a substance selected from the group consisting of a compound represented by the below general formula (I):



wherein X represents a connecting group whose number of atoms in a main chain is 2 to 5 (said connecting group may be substituted), A represents hydrogen atom or acetyl group, E represents an aryl group which may be substituted or a heteroaryl group which may be substituted, ring Z represents an arene which may have one or more substituents in addition to the group represented by formula -- O-A wherein A has the same meaning as that defined above and the group represented by formula --X--E wherein each of X and E has the same meaning as that defined above, or a heteroarene which may have one or more substituents in addition to the group represented by formula --O--A wherein A has the same meaning as that defined above and the group represented by formula -- X--E wherein each of X and E has the same meaning as that defined above. Unlike the instant claims, the reference claims are limited in scope to a method for preventive and/or therapeutic treatment of dermal conditions.

It would have been obvious to a person of skill in the art at the time the invention was made to treat a patient with any suitable cancer with the reference method comprising administering the identical compounds as recited in the instant claims for its anti-tumor effect. One would have been motivated to treat any cancer with said reference method because one would reasonably expect that administration of the same drug to the same (cancer) population would have the therapeutic effects. Thus, a person of skill in the art at the time the invention was made would have considered the instant claimed invention to be an obvious variant of the reference claims.

Claims 1, 29, and 34-41 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 13-14, 19-23, 25-30, 55-63 of copending US Patent Application No. 10/433,619, in view of Callahan et al. (US Patent 6,492,425). Unlike the instant claims, the reference claims are directed to a method of inhibiting activation of NF-kB comprising administering the identical instantly claimed compounds of formula 1. The above discussion of Callahan et al. is incorporated by reference. To reiterate, Callahan et al. teach inhibitory compounds of transcription factor NF-κB and methods of treatment of a variety of diseases associated with NF-κB activation in a patient in need of treatment thereof, including cancer (e.g. Hodgkin's disease) and restenosis, wherein the patient includes human (see abstract, and col. 3, line 17 to col. 4, line 54; see especially reference claim 1. It would have been obvious to a person of skill in the art at the time the invention was made to treat a patient with an NF-κB associated disorder (e.g. Hodgkin's disease) as taught by Callahan et al. with a reference compound to its anti-cancer effect. One would have been motivated to treat a

patient in need of treatment thereof with a reference compound because Callahan et al. teach NF-κB inhibitor drugs, wherein a major portion of the chemical structure of said drugs is identical to the reference compounds, which are useful for treating NF-κB associated disorders and drugs that have similar structures would reasonably be expected to exhibit similar therapeutic profiles. Thus, the instant reference claims are found to be an obvious variant of the reference claims.

These are provisional obviousness-type double patenting rejections because the conflicting claims of the copending applications have not in fact been patented.

Response to applicant's argument

Applicant's request to hold the nonstatutory obviousness-type double patenting rejections in abeyance pending a finding of allowable subject matter is acknowledged. However, since applicant has not substantially traversed the rejections, the rejections are maintained for the reasons of record

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

23 April 2009
/C. R./ Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611